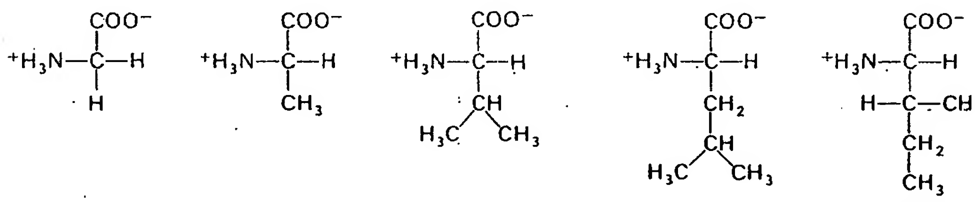
Appendix A

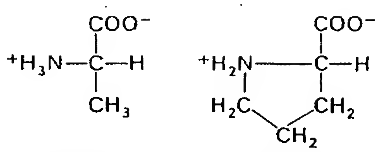
damental alphabet of proteins is at least two billion years old. The remarkable range of functions mediated by proteins results from the diversity and versatility of these twenty kinds of building blocks. In subsequent chapters, we will explore ways in which this alphabet is used to create the intricate three-dimensional structures that enable proteins to participate in so many biological processes.

Let us look at this repertoire of amino acids. The simplest one is glycine, which contains a hydrogen atom as its side chain (Figure 2-8). Alanine has a methyl group as its side chain. The other amino



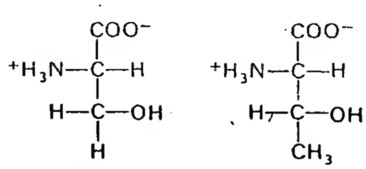
Glycine (Gly) | Alanine (Ala) | Valine (Val) | Leucine (Leu) | Isoleucine (Ile)

Figure 2-8
Amino acids having aliphatic side chains.



Alanine (Ala) | Proline (Pro)

Figure 2-9
Proline differs from the other common amino acids in that it has a secondary amino group.



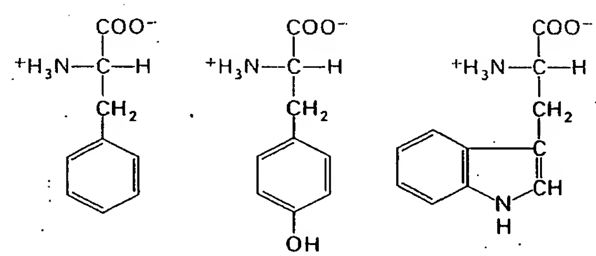
Serine (Ser) | Threonine (Thr)

Figure 2-10
Serine and threonine have aliphatic hydroxyl side chains.

acids that have hydrocarbon side chains are valine, leucine, isoleucine, and proline. However, proline differs from the other amino acids in the basic set of twenty in that it contains a secondary rather than a primary amino group (Figure 2-9). Strictly speaking, proline is an imino acid rather than an amino acid. The side chain of proline is bonded to both the amino group and the α-carbon, which results in a cyclic structure.

Two amino acids, serine and threonine, contain aliphatic hydroxyl groups (Figure 2-10).

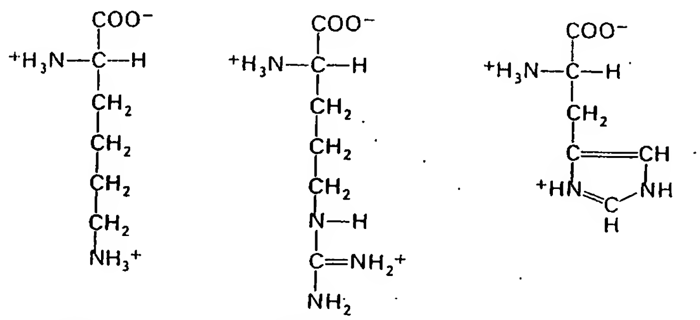
There are three common aromatic amino acids: phenylalanine, tyrosine, and tryptophan (Figure 2-11).



Phenylalanine (Phe) | Tyrosine (Tyr) | Tryptophan (Trp)

Figure 2-11
Phenylalanine, tyrosine, and tryptophan have aromatic side chains.

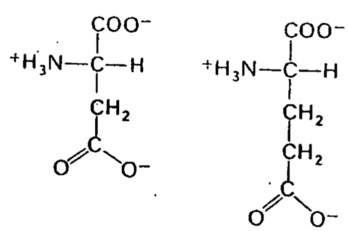
The side chains of the amino acids mentioned so far are uncharged at physiological pH. We turn now to some charged side chains. Lysine and arginine are positively charged at neutral pH, whereas whether histidine is positively charged or neutral depends on its local environment. These basic amino acids are shown in Figure 2-12. The negatively charged side chains are those of glu-



Lysine (Lys) Arginine (Arg) Histidine (His)

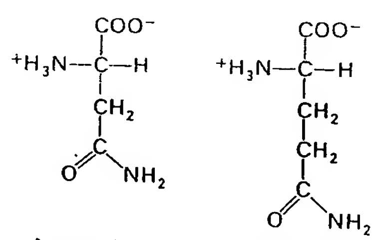
Figure 2-12
Lysine, arginine, and histidine have basic side chains.

tamic acid and aspartic acid (Figure 2-13). These amino acids will be called glutamate and aspartate to emphasize the fact that they are negatively charged at physiological pH. The uncharged derivatives of glutamate and aspartate are glutamine and asparagine (Figure 2-14), each of which contains a terminal amide group rather than a carboxylate. Finally, there are two amino acids whose side chains contain a sulfur atom: methionine and cysteine (Figure 2-15). As will be discussed shortly, cysteine plays a special role in some proteins by forming disulfide cross-links.



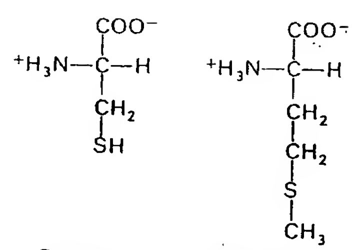
Aspartate (Asp) Glutamate (Glu)

Figure 2-13
Aspartate and glutamate have acidic side chains.



Asparagine (Asn) Glutamine (Gln)

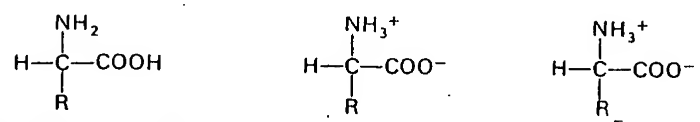
Figure 2-14
Asparagine and glutamine have amide side chains.



Cysteine (Cys) Methionine (Met)

Figure 2-15
Cysteine and methionine have sulfur-containing side chains.

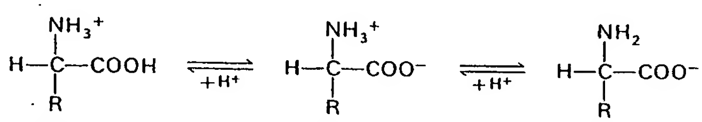
Amino acids are the basic structural units of proteins. An amino acid consists of an amino group, a carboxyl group, a hydrogen atom, and a distinctive R group bonded to a carbon atom, which is called the α-carbon (Figure 2-5). An R group is referred to as a *side*



Un-ionized form of an amino acid **Dipolar ion (or zwitterion) form of an amino acid** Side chain

Figure 2-5
Structure of the un-ionized and zwitterion forms of an amino acid.

chain for reasons that will be evident shortly. Amino acids in solution at neutral pH are predominantly *dipolar ions* (or *zwitterions*) rather than un-ionized molecules. In the dipolar form of an amino acid, the amino group is protonated ($—NH_3^+$) and the carboxyl group is dissociated ($—COO^-$). The ionization state of an amino acid varies with pH (Figure 2-6). In acid solution (e.g., pH 1), the



Predominant form at pH 1 **Predominant form at pH 7** **Predominant form at pH 11**

Figure 2-6
Ionization states of an amino acid as a function of pH.

carboxyl group is un-ionized ($—COOH$) and the amino group is ionized ($—NH_3^+$). In alkaline solution (e.g., pH 11), the carboxyl group is ionized ($—COO^-$) and the amino group is un-ionized ($—NH_2$). The concept of pH and the acid-base properties of amino acids are discussed further in the Appendix to this chapter.

The tetrahedral array of four different groups about the α-carbon atom confers optical activity on amino acids. The two mirror-image forms are called the L-isomer and the D-isomer (Figure 2-7). *Only* L-*amino acids are constituents of proteins.* Hence, the designation of the optical isomer will be omitted and the L-isomer implied in discussions of proteins herein, unless otherwise noted.

Twenty kinds of side chains varying in *size, shape, charge, hydrogen-bonding capacity, and chemical reactivity* are commonly found in proteins. Indeed, all proteins in all species, from bacteria to humans, are constructed from the same set of twenty amino acids. This fun-

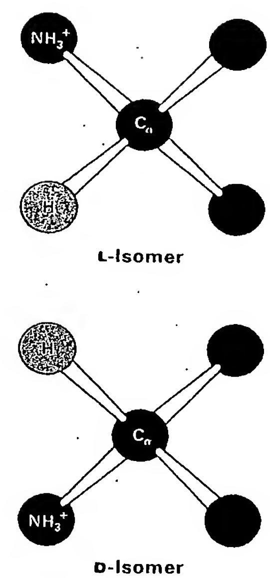


Figure 2-7
Absolute configurations of the L- and D-isomers of amino acids.